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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/311,720	05/14/1999	GREGORY M. GLENN	PM254809	1614

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/311,720	GLENN ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *62-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,9-12,14,28,30-44,47-61,80,81,87,90,93-96,98,99 and 102-136* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1, 2, 4, 9-12, 14, 28, 30-44, 47-74, 80, 81, 87, 90 93-96, 98, 99, 102-136.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 14, 2004 has been entered.

DETAILED ACTION

This application is a continuation-in-part of 08/749,164, filed November 14, 1996, now US Patent 5,910,306, which claims benefit to provisional application 60/086,196, filed My 21, 1998.

Applicants amendment filed January 14, 2004, has been received and entered. Claims 3, 5-8, 13, 15-27, 29, 45, 46, 78, 79, 82-86, 88, 89, 91, 92, 97, 100 and 101 are canceled. Claims 128-136 have been added. Claims 1, 4, 9-12, 14, 28, 30, 31, 35, 36, 39-41, 44, 55-58, 72, 80, 81, 87, 90, 93-96, 98 and 99 have been amended. Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-74, 80, 81, 87, 90, 93-96, 98, 99, 102-136 are pending.

Election/Restriction

Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-74, 80, 81, 87, 90, 93-96, 98, 99, 102-136 are pending. Claims 32-34, 37, 38, 42, 43, 47-54, 59-71, 73 and 74 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species of the

invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 21. Applicant has acknowledged the restriction requirement and believes that the present amendments to the generic claims has put the instant application in condition for allowance. See Applicants' amendment page 19, first full section.

Previously, the elected invention that was under examination was drawn to the elected species (i) the antigen sequestrin; (ii) the adjuvant CpG1; and (iii) and adenoviral regulatory region for the expression of the antigen. Upon a search of the relevant art for the new claim amendments references have been identified that address other species of antigen and vectors encompassed by the generic claims. Accordingly, because it would not constitute an undue burden to search and review the pending claims drawn to these species of embodiments, the restriction requirement is withdrawn with regard to the species of (i) the antigen and (iii) the vector. However, the restriction requirement is maintained with respect to the elected species of (ii) the adjuvant of a CpG.

Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-54, 62-74, 80, 81, 87, 90, 93-96, 98, 99, 102-136 are pending. Claims 62-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species of adjuvant, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement. Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-54, 80, 81, 87, 90, 93-96, 98, 99, 102-136 are currently under examination as they are drawn to the species CpG as an adjuvant.

Priority

Applicant argue that the instant claims are in compliance with the requirements of 35 U.S.C. 112, first paragraph, pointing to specific support in the previous parent applications for the generically claimed invention. Applicants' response and arguments have been fully considered, and not found persuasive.

The present invention is drawn to methods and formulations which are first presented in the instant application. Specifically, the prior applications 80/749,164, now US Patent 5,910,306, and provisional application 60/086,196 all provide guidance for methods and formulations for the delivery of an antigen and adjuvant by transdermal delivery. Review of the priority documents provides teaching only for molecules that are antigens themselves, not for antigens that are produced by DNA vectors. Review of the priority documents provides no literal nor figurative support for the delivery of DNA vectors. Moreover, the specific guidance provided in the priority documents is directed to only specific characteristics of antigen molecules that are to be delivered, and are not applicable to the characteristics of DNA for delivery. The only mention of recombinant methodology in the priority documents is in the context of providing the antigen that is to be delivered. In addition, the priority documents provide general and specific guidance for various specific types of adjuvant, however, there is no literal nor figurative support that the use of CpG was contemplated. In summary, the priority documents relied upon by Applicants fail to adequately support the instantly claimed method. As noted in the previous office action, a later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the

parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). In this case the prior applications provide support for the delivery of an antigen to a subject, however fail to provide literal or figurative support the instantly claimed invention as it is drawn to the delivery of DNA wherein an antigen is produced by the cells of the subject. Thus, while the transdermal delivery of antigen vaccines are supported in the prior applications, DNA vaccines and the methods and consideration of using these vaccines are not.

Claim Objections

The claims are objected to because of the following informalities: As noted above the restriction requirement is withdrawn with regard to the species of (i) the antigen and (iii) the vector. However, the restriction requirement is maintained with respect to the elected species of (ii) the adjuvant CpG. The generic claim to any antigen has not been found allowable, therefore the claims should be amended to reflect the elected species of adjuvant.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-54 , 80, 81, 87, 90, 93-96, 98, 99, 102-127 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing an immune response in a mammal comprising the steps : providing a polynucleotide construct comprising an adenoviral regulatory region operatively linked to a polynucleotide encoding sequestrin; administering said construct to a mammal wherein administration results in the expression of said construct and production of a sequestrin protein, does not reasonably provide enablement for a method of immunization is withdrawn.

Amendments to the claims and withdrawal of the restriction requirement has rendered the basis of the rejection moot. As noted in the previous office actions, the art supports that any antigen expressed in a subject, even sequestrin, will provide an antigen for the immune system of a subject and result in inducing an antigen specific response. It is noted that claim124 specifically recites that the response is protective, which is counter to the results and arguments provided for sequestrin. However, it would not constitute undue experimentation to use and express known antigens, or to test potential antigens for their ability to provide some protective affect against a given antigen.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4, 9-12, 14, 28, 30-44, 47-54, 80, 81, 87, 90, 93-96, 98, 99, 102-136 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang *et al.* (US Patent 6348,450 B1).

Tang *et al.* provide methods and materials for genetic immunization using DNA vectors. The methods taught by Tang *et al.* comprise a non-invasive method wherein the DNA vector is provided to the surface of the skin. Tang *et al.* provide general and specific guidance for the types of antigens to be expressed and specific guidance for the types of vectors for the expression. Tang *et al.* teach that vectors can be delivered alone, or in combinations with other agents that will aid in the transfection of a cell. Finally, Tang *et al.* teach that additional agents can be provided to augment the immune response, and specifically teach that CpG rich sequences can be used together with the transcription/translation signals necessary for expression (column 16, lines 25-36).

Claims 1, 2, 4, 14, 28, 30-44, 47-54, 80, 81, 87, 90, 93, 94, 96, 98, 99, 102-136 are rejected under 35 U.S.C. 102(e) as being anticipated by Kreig *et al.* (US Patent 6,339,068).

Kreig *et al.* teach methods and materials for immunization protocols for the delivery and expression of polynucleotide vectors. Kreig *et al.* primarily detail the use of CpG sequences as an adjuvant, however provides multiple context in which the CpG sequence can be used for genetic immunization. Included in the methodology for delivery, Kreig *et al.* teaches that transdermal delivery can be used, specifically citing methods provided in the references of Fynan, Tang, Fuller and Keller (column 10, lines 34-60). Kreig *et al.* provides detailed guidance on specific vectors and promoters, and various formulations for the delivery of the DNA vaccines.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 9-14, 19-26, 28, 30-44, 47-77, 80, 81, 87, 90, 93-96, 98, 99, 102-136 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khavari *et al.* (US Patent 6,087,341) in view of Krieg *et al.* ('068).

It is noted that claims 102-116 represent copies of claims 1-15 of Khavari *et al.*, however the elected species of adjuvant of CpG currently under examination is not taught by Khavari *et al.* Accordingly, Khavari *et al.* is not provided as a 102 type reference because it fails to teach all the limitations encompassed by the claim. However, Khavari *et al.* does teach transdermal methods of the delivery of polynucleotide vectors to generate an immune response in a subject. Khavari *et al.* teaches a variety of antigens and vectors that can be used, and provides various formulations for the transdermal delivery of the polynucleotide. In addition, Khavari *et al.* teach that other agents can be used to augment the immune response however Khavari *et al.* does not teach the use of CpG as an adjuvant. Kreig *et al.* teach methods and materials for immunization

protocols for the delivery and expression of polynucleotide vectors. Kreig *et al.* primarily detail the use of CpG sequences as an adjuvant, however provides multiple context in which the CpG sequence can be used for genetic immunization. Included in the methodology for delivery, Kreig *et al.* teaches that transdermal delivery can be used, however does not provide specific details on the practice of this methodology.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the detailed teachings for transdermal delivery of a polynucleotide as taught by Khavari *et al.* to affect the methods of Kreig *et al.* One having ordinary skill in the art would have been motivated to use the methods of Khavari *et al.* because of the specific motivation provided by Kreig *et al.* to use transdermal delivery. There would have been a reasonable expectation of success to use the methods of transdermal delivery taught by Khavari *et al.* with the materials taught by Kreig *et al.* given the results of both Khavari *et al.* and Kreig *et al.* demonstrating the success of the methodology and materials detailed in each of the disclosures.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Applicants' request for a declaration of interference is noted, however the pending claims have not been found allowable. Moreover, as discussed in the section regarding the priority of the instant application, even if subject matter for transdermal DNA vaccination was found

allowable, the instant application only would have the effective filing date as of its own filing date. Accordingly, the instant application would not predate the US patents issued to Khavari *et al.* and Tang *et al.* indicated in Applicants' request.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

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